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**Multiple sclerosis: Long-term outcomes in ethnic minorities with MS: analysis of a UK population-based registry.**

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## **Abstract**

**Background:** Multiple sclerosis (MS) is most frequent in Caucasian populations. However, studies of MS in other ethnic groups may offer unique insights into genetic and environmental influences on disease, and data on long-term outcomes in these patients is limited. We have investigated clinical features and time to disability milestones in ethnic minority (EM) patients with MS in a UK population and made comparisons to a Caucasian cohort from the same region.

**Methods:** 1949 MS patients (1866 Caucasian, 83 EM) were identified from a regional disease registry. Cox proportional hazards regression was used to analyse time to EDSS 3.0, 4.0 and 6.0.

**Results:** EM patients were younger at disease onset (28.6 years versus 32.8 years,  $p=0.001$ ), and PPMS was less common (EM: 4.8%, Caucasian: 11.6%,  $p=0.03$ ). After correction for clinical variables, ethnicity was associated with time to EDSS 3.0 (EM: hazard ratio [HR] 1.75,  $p<0.0001$ ) and 4.0 (HR 1.46,  $p=0.03$ ), but not 6.0 (HR 1.5,  $p=0.05$ ).

**Conclusions:** EM patients reach early levels of fixed disability more rapidly than Caucasian patients, but this effect diminishes at later stages of disease. This has implications for clinical management of these patients.

## **Introduction**

Multiple sclerosis (MS) is most common in Caucasian populations. A few studies have attempted to examine MS in ethnic minority (EM) groups but have struggled to make effective comparisons because of small patient numbers, lack of comparative data, limited follow-up and additional confounding factors. In addition, analysis[1–10] has focused on early phases of disease,[1] cross-sectional analysis,[2,8–10] or specific subgroups.[3,5] Few have examined long-term outcomes,[4,6,7] and none of these have compared with a geographically matched Caucasian population. However, differences in disease frequency and phenotype may provide key insights into disease aetiology and disease trajectory. We have examined patterns of early disease and long-term outcomes in EM and Caucasian patients from a well-described population-based cohort from the United Kingdom.

## **Methods**

### Patient selection

The southeast Wales MS registry was established in 1985 from a cross sectional study[11] with prospective longitudinal data collected since 1999. Patients were included if they had a diagnosis of MS, ethnicity was recorded, and prospectively collected longitudinal data was available from disease onset, including relapses, disease course, and Expanded Disability Status Scale (EDSS)[12] scores. EM patients were also classified by place of birth. The South East Wales Ethics Committee approved the study (reference number 05/WSE03/111) and written informed consent is obtained from all patients.

### Statistical analysis

Demographics and clinical features at disease onset were compared using chi-squared tests, Student's t test and one-way ANOVA. Time to EDSS 3.0, 4.0 and 6.0 was analysed using Cox proportional hazards regression, adjusting for age at onset, sex, and initial disease course. All analyses were undertaken using SPSS version 21.

## **Results**

### Demographics and clinical features

1866 Caucasian and 83 EM patients were identified (22 Afro-Caribbean, 48 Asian, and 13 Middle Eastern). 27 EM patients were born in Europe and 35 elsewhere. Country of birth was not available in 21.

Male:female ratio was similar in both groups (EM: 1.7:1, Caucasian: 2.3:1,  $p=0.10$ ). EM patients were younger at disease onset (28.6 years versus 32.8 years,  $p=0.001$ ). There was no difference in demographic features between EM subgroups or by country of birth.

PPMS was less common in EM patients (EM: 4.8%, Caucasian: 11.6%,  $p=0.03$ ). There was no difference in annualised relapse rates (EM: 0.65, Caucasian: 0.55,  $p=0.08$ ), or for symptoms at disease onset (Figure 1). No difference was identified for any clinical features between EM subgroups or by country of birth.

### Prognosis

50 EM and 1417 Caucasian patients reached EDSS 3, 39 EM and 1313 Caucasian patients reached EDSS 4.0, and 28 EM and 1048 Caucasian patients reached EDSS 6.0. Age at onset

was associated with all endpoints, and disease course with time to EDSS 4.0 and 6.0. Ethnicity was associated with time to EDSS 3.0 (EM: hazard ratio [HR] 1.8 (1.3 – 2.3),  $p < 0.0001$ ), and 4.0 (EM: HR 1.5 (1.0–2.0),  $p = 0.03$ ). However this effect was not significant for time to EDSS 6.0 (EM: HR 1.5 (0.99–2.2),  $p = 0.05$ ) (Table 1).

## Discussion

In this study we have identified a younger age at onset and reduced frequency of PPMS in EM patients, with no differences observed in other presenting features. We also identified differences by ethnicity in reaching EDSS 3.0 and EDSS 4.0, although this effect did not persist in later stages of disease.

The reason for the difference in outcomes is not clear, but could be genetic or environmental, or a combination of the two. It may also reflect variation in socioeconomic status, particularly for immigrants. The fact that the differences seen were limited to the earlier phases of disease is intriguing although larger studies are needed to confirm whether this was a power limitation at EDSS 6.

Early studies suggested a poorer outcome for African Americans with MS,[1,2,5] but these studies were limited by cross-sectional analysis methods and the inclusion of patients with optico-spinal MS, before neuromyelitis optica was recognised as a separate disease. More recent studies have found a time to EDSS 6.0 of 22 years in Hong Kong Chinese,[6] 25 years in Lebanese[4] and 26 years in Brazilian patients,[7] which are at the upper end of estimates in Caucasian populations.[13] Additionally a recent comparative study of Japanese and British patients with MS has shown a reduced frequency of PPMS and a lower MS severity score (MSSS) in Japanese patients, implying a better outcome than in British patients.[10]

For future studies, detailed data on family ancestry and geographical origin may be informative with regards to potential genetic admixing with different European populations, particularly in those of Afro-Caribbean descent. This information was not available for our cohort but would be of value in future studies.

Limitations of our study included the inability to examine outcomes in specific ethnic sub-groups as a result of limited patient numbers, the representation of only three EM groups and the lack of detailed long-term outcomes at very high disability score (i.e. EDSS 8.0 and death) which may have been informative. Defining differences in outcomes would clearly be of value in informing patient management in EM but is only likely to be achieved by the interrogation of very large combined datasets and would be an important future direction of research.

In conclusion, our study suggests that presenting features for patients with MS residing in a common geographical location is similar across ethnic groups. However, EM patients present earlier and accumulate early disability more rapidly than their Caucasian counterparts. These observations may be of importance for disease management in EM patients, in particular when considering early efficacy of disease-modifying therapies.



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## Figures

Figure 1: Symptoms at disease onset

## Tables

Table 1: Cox proportional hazards regression model

Clinical variable	EDSS 3.0		EDSS 4.0		EDSS 6.0	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Ethnicity: Caucasian EM	Reference 1.75 (1.32–2.33)	<0.001	Reference 1.46 (1.05–2.02)	0.026	Reference 1.47 (0.99–2.16)	0.05
Age at onset	1.04 (1.04–1.05)	<0.001	1.04 (1.04–1.05)	<0.001	1.05 (1.04–1.06)	<0.001
Sex	0.97 (0.86–1.08)	0.54	0.96 (0.85–1.09)	0.54	0.96 (0.84–1.10)	0.52
Disease course	0.85 (0.72–1.00)	0.05	0.74 (0.62–0.88)	0.001	0.58 (0.48–0.69)	<0.001